Remarks

Applicant thanks Examiner Barnhart for the telephone interview on September 23, 2008. During the call, the undersigned and Examiner discussed the inventions set forth in the application, the currently pending claims, and the currently cited references. In light of this conversation, Applicant submits the Amendments and Arguments contained in this Response.

This paper is being provided in Response to the Office Action mailed June 3, 2008, for the above-referenced application. Claims 1, 3, 21, 29-31, 56 have been amended. Claims 83 and 84 have been cancelled, without prejudice. Applicant respectfully submits that the amendments to the claims do not add new subject matter.

Claim Rejections under 35 U.S.C. § 112

Examiner has rejected claims 1, 3, 6, 12, 21, 22, 25-31, 56, 57 and 82-84 under 35 U.S.C. § 112, first or second paragraph. Claims 1, 3, 21, 29-31 have been amended, and Claims 83 and 84 have been cancelled.

The Examiner states that, with respect to Claim 3, the specification is enabling for a composition that repairs or restructures tissue when administered to an organism, but does not reasonably provide enablement for a composition that replaces tissue per se. Examiner further states that Claim 3 is drawn in part to a composition that replaces tissue in an organism, tissue comprises an aggregate of cells and their supportive matrix by definition, therefore, a composition that replaces tissue necessarily includes cells. Examiner states that Claim 1 does not include cells, and the specification does not appear to contemplate embodiments in which cells are placed into the instantly claimed composition, and therefore, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention across its entire scope. Applicant has amended Claim 3 to clarify that which is claimed.

Examiner states that Claim 1 is confusing because it is unclear whether the photopolymerizable monomers and the material insoluble by the monomers "that is a solid at below the body temperature of a living organism and a gel at a body temperature of a living organism" responds to light, temperature, or both. Claim 1 has been amended to clarify that which is claimed.

Examiner states that Claim 1 is also confusing because the nature and extent by which the insoluble material "shields the bioactive molecules from a polymerization process" is unclear. A polymerizing environment exposes bioactive molecules to various sources of degradation – including but not limited to heat, initiators or initiators plus accelerators in excited states, or anionic, cationic or radical species. One of ordinary skill in the art would understand the language in Claim 1, in light of the specification, to provide for insoluble material that shields or blocks the bioactive molecules from a polymerizing environment to the nature or extent that the bioactive molecules are not accessible to degradative or denaturing environments. *See, e.g.,* Table 2, page 16 and Exemplification – Retention of Enzymatic Activity and Enzyme Characterization, pages 15-17. At the time of invention, the Maldi-TOF (fact of error of 0.01%) was the appropriate equipment to use to determine a modification, if any, of proteins. Table 2 shows that the molecular weight of protected enzymes (after being exposed to the polymerizing environment and after being released out of the cross-linked polymer created by polymerization) was closer to the ones of the native forms (not exposed to the polymerizing environment, and not released out of the cross-linked polymer produced by polymerization). In contrast, the molecular weight of unprotected enzymes (after polymerization) suffered a change. This change, although expressed as a percentage, may seem small, but correlates to a significant biological activity loss. *See also* page 20, lines 3-4 and 13-19 which discusses the observation of damage to the bioactive molecules caused by photo-polymerization. Applicant has amended Claim 1 to make clear that which is claimed and respectfully submits that the scope of the claim is supported by the originally filed specification.

Examiner further states that Claim 1 is unclear because the conditions for cross-linking the monomers to form a polymer is not limited in the claim. Claim 1 has been amended to make clear that which is claimed.

The deficiencies noted by Examiner in Claims 83 and 84 are moot because Applicant has cancelled those claims.

Examiner states that Claim 3 is unclear because it allows that the composition can "replace" tissue in an organism, there are no cells in the composition, and cells cannot reasonably be considered "bioactive molecules." Claim 3 has been amended and addressed above.

Examiner states that Claim 31 is indefinite for reciting a use without any active, positive steps delimiting how this use is actually practiced because the claim requires that the photo-polymerization in Claim 30 "uses visible radiation" without setting forth any steps involved in the method/process. Applicant submits that Claim 31 is definite, but has amended the claim to further make claim that which is claimed.

Examiner states that Claims 83 and 84 require further amendment. Applicant has cancelled those claims.

In light of the above comments and amendments to the claims, Applicant respectfully requests that the pending U.S.C. § 112 rejections be reconsidered and withdrawn.

Claim Rejections under 35 U.S.C. § 103

Claims 1, 3, 6, 12, 21, 22, 25-31, 56, 57 and 82-84 remains rejected under 35 U.S.C. § 103 as being unpatentable over Evans et al. (U.S. Patent Publication No. 2003/0236573 A). Claims 1, 3, 21, 29-31 have been amended, and Claims 83 and 84 have been cancelled.

The Examiner states that Evans teaches a flowable implant for treating tissue defects, which may include a growth factor (*i.e.,* a bioactive protein), gelatin (which is both an insoluble material and a bioactive protein), and a photopolymerizable monomer (*e.g.,* FOCALSEAL) (*see* paragraph 139). The Examiner further states that Evans contemplates an embodiment in which the implant treats a tissue defect only at body temperature (paragraphs 127 and 139), and may further include polyethylene glycol as a filler (Table 4 at paragraph 7) and may include plasticizers other than polyethylene glycol, many of which are also cross-linked synthetic polymers (Tab 5 at paragraph 108). The Examiner continues that the composition of Evans inherently comprises light, *i.e.,* the light in the laboratory in which it is prepared.

The disclosure of Evans is directed towards a bone plug or implant that is suitable to be delivered and inserted into a defect in the bone of a living being for purposes of repairing/regenerating the same. *See, e.g.,* [0001], [0009], [0042] of Evans. The preferred embodiments throughout Evans are directed to implants comprising native fibrous collagen that delivers one or more biologically active agent to the bone defect. *See, e.g.,* [0081]-[0085], [0087]-[0089], [0091] of Evans. While Evans discloses a "flowable" material to be used as an implant that "could also photopolymerize like FocalSeal (Focal, Inc., Lexington, Mass.)," that

"flowable" material is disclosed or suggested to be a catalyst for adhesion of the plug or implant material to itself, to preclude the plug or implant material from leaking out of the patient. *See* [139] of Evans ("The flowable material can be designed to harden slightly after placement, like an epoxy or silicon caulking material, so that it is not extruded from the puncture during tissue movement or flexing."). Notably, FocalSeal is not listed in any of the tables of Evans. The FocalSeal photopolymerizable reference is not a disclosure, teaching or suggestion of the substrate system presently claimed, comprising a photo-polymerized cross-linked polymer, wherein the polymer comprises bioactive molecules and a material insoluble by the polymer and wherein the insoluble material shields the bioactive molecules from degradation caused by a photo-polymerizing environment, and transitions from a solid to a gel at or above approximately the body temperature of a living organism.

Unlike Evans, the presently amended claims address a concern that a polymerizing environment is deleterious to reactive molecules entrapped within the matrix, and therefore include an insoluble material that shields the bioactive molecules from the polymerizing environment. *Id.* Evans does not provide any structural limitations for overcoming the deleteriousness of the polymerizing environment, as the present application sets forth. While Evans mentions that the material could "contain drugs or other agents" (*i.e.,* bioactive molecules [0139] of Evans), there is nothing in Evans or in the knowledge of one of ordinary skill in the art to suggest that the implant material as described by Evans can be polymerized without incurring a deleterious effect on the activity of the bioactive molecules.

Based on the above, Evans does not disclose, teach or suggest the amended claims of the present invention. Applicant therefore respectfully submits that Evans does not render the claims obvious, and respectfully requests that this rejection be reconsidered and withdrawn.

Claims 29, 56 and 84 are rejected under 35 U.S.C. § 103 as being unpatentable over Evans as applied to Claims 1, 3, 6, 12, 21, 25-28, 30, 31, 57, 82 and 83, and further in view of Kaetsu et al. (U.S. Patent No. 4,359,483). Claims 1, 3, 21, 29-31 have been amended, and Claims 83 and 84 have been cancelled. Kaetsu does not remedy the deficiencies of Evans. Applicant respectfully submits that Kaetsu does not disclose, teach or suggest the amended claims of the present invention, alone or in combination with Evans. Applicant therefore

respectfully submits that Evans, in view of Kaetsu, does not render the claims obvious, and respectfully requests that this rejection be reconsidered and withdrawn.

Based upon the above, Applicant respectfully requests that the Examiner reconsider and withdraw all outstanding rejections and objections. Applicant again thanks the Examiner for her time during the telephone interview and subsequently considering these Amendments and Remarks. Favorable consideration and allowance are earnestly solicited. Should there be any questions after reviewing this paper, the Examiner is invited to contact the undersigned at 617-248-4054.

Respectfully submitted,

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